REMARKS

Status of the Claims

Claims 1–30 were pending prior to entry of the present amendment.

Claims 1–15 are canceled herein without prejudice or disclaimer.

Interview Summary

Applicants would like to thank the Examiner for the courtesy of a telephonic interview with Applicants' representative Jonathan Ball on August 11, 2008. During the interview, the Examiner clarified the basis for the obviousness rejections and explained that the Office views the use of siRNA to inhibit expression of a know mRNA sequence as prima facie obvious under the holding of KSR v. Teleflex, 127 S. Ct. 1727 (2007), absent a showing of unexpected results or a teaching away from using a specific siRNA sequence, in view of various publications and tools which allegedly were available to aid in the identification of suitable siRNA sequences. As discussed during the interview, Applicants identify in this paper specific disclosures in the art cited by the Examiner teaching away from the use of the claimed siRNA duplexes.

Claim Rejections

35 U.S.C. §112, ¶ 1

The Examiner has rejected claims 1–3 and 5–15 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that "'tyrosinase' embraces a genus of sequences" and Applicants have "not closed mouse or human 'tyrosinase' to any single sequence in the claims." Applicants respectfully traverse the rejection on the grounds that one skilled in the art would have been directed to the native human and mouse mRNA sequences which were well-known in the art at the time the application was filed. Nevertheless, the rejection is now moot in view of the present amendments.

35 U.S.C. §102(e) and 35 U.S.C. §103(a)

The Examiner has maintained the rejection of claims 1–3, 5–9, 14 and 15 under 35 U.S.C. §102(e) as being anticipated by Bennett et al. (US Patent Pub. 2004/0215006) as well as the rejection of claims 1–3 and 5–15 under 35 U.S.C. §103(a) as unpatentable over Bennett et al. in view of Mahashabde et al. (US 6,436,378) and Perricone (US 2002/0141956). The Examiner

also makes a new rejection of claims 1–30 over the same combination, further in view of "Ambion siRNA target finder." Applicants respectfully traverse the rejection.

The maintained §102 rejection over Bennett and the maintained §103 rejection over Bennett in view of Mahashabde and Perricone are rendered moot due to the cancellation of claims 1-15. However, Applicants submit that those claims fully distinguish the cited combination of reference for reasons already of record and reserve the right to pursue the canceled subject matter in a continuing application.

The Examiner contends that the Ambion siRNA target finder provides a duplex comprising SEQ ID NOs: 1 and 2 upon entry of the human tyrosinase mRNA sequence (GenBank M27160.1) and that it would have been obvious to use the generated duplex in the method of Bennett. Applicants traverse this rejection.

As an initial matter, Applicants submit that the rejection is deficient because the Examiner has not established that the Ambion siRNA target finder would have produced the same results prior to the December 17, 2003 filing date as obtained by the Examiner on June 18, 2008. The Examiner merely notes that the Ambion tool was "available 2002 to the public," but this in itself is not sufficient to support the ground of rejection because the Ambion web site is not relevant absent evidence that the query results would have been the same prior to Applicants' filing date. For example, the Examiner refers to "the Ambion algorithm" but does not attempt to show that that algorithm has not been modified since 2003. Applicants submit that this is analogous to finding an article for sale on eBay® in 2008 and contending that the same article must have also been on sale in 2003, since the eBay® website was available to the public in 2003. For this reason alone, Applicants believe that the rejection is deficient.

In any event, assuming that the Ambion siRNA target finder would have returned SEQ ID NOs: 1 and 2 prior to Applicants' filing date, there would have been no motivation to select this particular siRNA duplex from the **139** siRNA duplexes that comprise the result set, particularly in view of the fact that the Ambion website **taught away** from selecting this duplex. When the human tyrosinase mRNA sequence (GenBank M27160.1) is entered into the Ambion tool, a result set comprising 139 siRNA duplexes is obtained, of which SEQ ID NOs: 1 and 2 are given in target sequence 46. See Exhibit 1. There is nothing that would have directed the skilled artisan to this particular sequence from the 139 other possibilities. Even if the Ambion website

constituted a disclosure of SEQ ID NOs: 1 and 2 (which it does not), it would not constitute a disclosure of legal sufficiency to direct one skilled in the art to the particular sequence claimed. See In re Ruschig, 379 F.2d 990, 154 USPQ 118 (CCPA 1967) ("something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required" to constitute a legally sufficient disclosure of a particular species).

Moreover, the Ambion website taught away from selecting "target sequence 46" from the 139 target sequences in the result set. The Ambion siRNA target finder "Information" page states that "G/C content is calculated and displayed because Ambion researchers have found that siRNAs with lower G/C content (30-50%) are more active than those with higher G/C content. If desired, you can choose to limit your siRNA choices by maximum G/C content." See Exhibit 2. For the Examiner's reference, Applicants have attached a printout of the "Information" page as it appear on October 9, 2003 -- just prior to the filing date of the instant application -- obtained from an Internet archival service (http://web.archive.org). See Exhibit 3. As shown, the Ambion "Information" page contained the identical teaching at the time the application was filed. This would have led one skilled in the art away from selecting target sequence 46 because that sequence has a "GC content" of 52.4%. In fact, if one sets the parameter "G/C content maximum (optional)" to 50% in the Ambion tool pursuant to this teaching, a result set of 120 target sequences is obtained which does not include target sequence 46. See Exhibit 4. Thus, target sequence 46 is one of 19 sequences in the 139 sequence result set that the Ambion tool would have suggested is less active than the others.

The Ambion site **teaches away** from selecting target sequence 46 for an additional reason. Specifically, the "Information" page, as it as it appeared on October 9, 2003 [Exhibit 3] states that:

> Below each candidate target, you will find a link to perform a BLAST search on the sequence. BLAST settings are preset to the recommended default for short sequences and can be modified as you choose (for more information, see the Blast tutorial). You may elect to BLAST the entire genome, or perform a more restricted search against sequences from your target species. **Choose siRNAs with fewer than 16–17 contiguous base pairs of homology to other genes in your target cells**. (emphasis added)

A BLAST search was performed for target sequence 46 by setting the database to "Human genomic + transcript" to look for homologies to other human genes. The results show that target sequence 46 has substantial homology -- i.e., 16 or more contiguous base pairs -- to other human genes. See Exhibit 5. For example, results show that target sequence 46 shares 17 contiguous base pairs with "Homo sapiens olfactomedin 4 (OLFM4), mRNA." The Ambion Information page therefore directly **teaches away** from selecting target sequence 46.

Accordingly, Applicants submit that the duplex defined by SEQ ID NOs: 1 and 2 would not have been obvious at the time the application was filed because the Examiner has offered no basis for selecting that duplex from the 139 duplexes produced by the Ambion tool, particularly in view of the fact that the Ambion site teaches away from using sequences with a G/C content over 50% and teaches away from using siRNA having more than 16 contiguous base pairs of homology with other human genes. Nothing in the Mahashabde and Perricone reference teaches or suggests the use of SEQ ID NOs: 1 and 2 for inhibiting the production of tyrosinase and therefore those reference cannot rectify the deficiencies of Bennett and the Ambion siRNA tool. Therefore, Applicants submit that the rejection under 35 U.S.C. §103(a) should be withdrawn.

While the elected species is the duplex defined by SEQ ID NOs: 1 and 2, a few observations are offered with respect to the remaining species. In particular, it is noted that SEQ ID NOs: 3 and 4 are also given in the Ambion result set as target sequence 79. See Exhibit 1. However, the Ambion site similarly **teaches away** from selecting target sequence 79 because the BLAST search for target sequence 79 using the "Human genomic + transcript" database shows that target sequence 79 shares 16 contiguous base pairs with, inter alia, "Homo sapiens annexin A5 (ANXA5), mRNA" and 16 contiguous base pairs with "Homo sapiens zinc finger protein 397 (ZNF397), mRNA." The relevant pages from this BLAST report as provided in Exhibit 6. The Ambion Information page therefore directly teaches against selecting target sequence 79 and thus the claimed siRNA defined by SEQ ID NOs: 3 and 4 also distinguish over the instant combination of references. The cited combination of art also has no relevance to the siRNA duplex defined by SEQ ID NOs: 5 and 6, inasmuch as it is not listed in the result set produced by the Ambion siRNA target finder. See Exhibit 1.

It is therefore believed that all of the claimed siRNA species are patentable over the Bennett in view of Mahashabde, Perricone, and the Ambion siRNA target finder. Applicants therefore submit that an action passing this case to allowance is warranted.

CONCLUSION

Based on the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

Respectfully submitted,

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By: /Joan M. McGillycuddy/
Joan M. McGillycuddy
Registration No. 35,608

Correspondence Address:
Avon Products, Inc.
Avon Place
Suffern, New York 10901
(845) 369-2114 Telephone
(845) 369-2900 Fax